(SLE) (8%). Twenty-seven patients received allogeneic HCT (alloHCT) for SSC (n=7), amyotrophic lateral sclerosis (n=6), autoimmune cytopenias (n=6), SLE (n=2), autoimmune enteropathy (n=1) and unclassified AI (n=3). The median age at HCT did not differ by transplant type (41 vs. 36 years for autoHCT and alloHCT, respectively) and most patients (66%) had a good performance score at HCT. The median time from diagnosis to transplant was 58 and 34 months for autoHCT and alloHCT, respectively. Irradiation-containing conditioning regimens were used in 109 cases (61%) and cyclophosphamide either alone or in combination with other agents without irradiation in 45 cases (25%). Most autoHCT recipients received total body irradiation, cyclophosphamide and anti-thymocyte globulin (64%). Peripheral stem cell cells were the predominant graft type; and 56% of these grafts were manipulated ex vivo (CD34+ cell selection or T-cell depletion). The probabilities of 100-day mortality were 10% (95% confidence interval [CI], 6-15%) and 17% (95% CI, 5-35%) after autoHCT and alloHCT, respectively. Corresponding one-year probabilities of overall survival were 89% (95% CI, 83-93%) and 75% (95% CI, 54-91%). One-year probability of overall survival post-autoHCT were 96%, 82% and 73% for MS, SSC and SLE respectively. In summary, these collective data from CIBMTR, MS and SSC are the most common autoimmune disease indications for HCT.

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AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION (AHSCT) FOR EARLY ONSET TYPE I DIABETES MELLITUS

Moraes, D.A.[1], Oliveira, M.C.[1], Stracieri, A.B.[1], Couri, C.E.[1], Barros, G.M.[1], Pieroni, F.[1], Coutinho, M.A.[1], Foss, M.C.[1], Simoes, B.P.[1], Voltarelli, J.C.[1] [1]Hospital das Clinicas/University of Sao Paulo, Ribeirao Preto, São Paulo, Brazil.

Introduction: Type I Diabetes mellitus (DM1) is an autoimmune disease that destroys pancreatic islet cells were insulin is producted, leading to insulin dependence and chronic complications such as retinopathy, nephropathy, neuropathy and coronary atherosclerosis.

Objectives: Evaluate the efficacy and toxicity (phases I/II) of high-dose cyclophosphamide (Cy) and rabbit anti-thymic globulin (rATG) followed by rescue with AHSCT in patients with less than 6 weeks from diagnosis of type 1 Diabetes mellitus.

Materials and Methods: Stem cells were mobilized from the bone marrow with Cy (2g/m^2) and Filgrastim (10μg/kg/d SC), collected by leukapheresis and cryopreserved. Patients were conditioned with Cy (50mg/kg x 4) and rATG (4.5 mg/kg), followed by stem cell infusion.

Results: Since December 2003, 15 patients were enrolled in this study. The medium age was 19.2 years, (14- 31 years), and the time between diagnosis and mobilization was 34.7 days (24 to 49 days). The mean hospitalization period was 24,2 days (16- 57 days) and the average number of CD34+ infused cells was 10.8×106/kg (5.8- 23.19×106/kg). Neutrophil engrafted on days 8 to 10 (average of 9,3 days) and platelets engrafted on days 0 to 15 days (average 12.3 days). There were no deaths. Most patients had neutropenic fever, but only one developed serious complications needing intensive care due to bilateral pneumonia, reversed with antibiotic therapy and non-invasive ventilation. All patients were using exogenous insulin therapy before mobilization, with an average dose of 0.38 Ul/kg (0.13 to 0.58 Ul/kg). In a mean follow-up of 14.2 months (1- 31 months), insulin therapy was suspended in 12 patients from D-7 to D+39 (average +32), two patients decreased insulin dose (16 and 21% compared to the period before AHSCT) and one patient remains using high dose insulin (1.7 Ul/kg/d). This last patient was the only one that presented ketoacidosis pre-AHSCT and received corticosteroids in the pre-conditioning period. Six to twelve months after AHSCT, the peptide-C levels considerably increased in 7 patients with clinical response and glycated hemoglobin values are <7%.

Conclusion: These results indicate that high-dose immunosuppression associated with AHSCT may induce prolonged clinical remission of Type 1 diabetes mellitus, without significant toxicity. The durability of response will be evaluated in longer follow-up.

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SERIAL SKIN BIOPSIES DEMONSTRATE REDUCED DERMAL FIBROSIS AFTER AUTOLOGOUS HEMOPOIETIC STEM CELL TRANSPLANT (A-HSCT) FOR SEVERE SYSTEMIC SCLEROSIS (SSS)

Shulman, H.M.[1], Nash, R.A.[1] [1]Fred Hutchinson Cancer Research Center, Seattle, WA.

Background: In a multiinstitutional study, 34 patients with SSS received high-dose immunosuppressive therapy followed by A-HSCT. Serial evaluations included improvement in the modified Rodnan skin score (mRSS, 51-0) and histologic dermal fibrosis score (DFS), grades 0-5.

Methods: 10 patients had 23 pre and post HSCT serial biopsies, mean follow-up 4 years. Punch biopsies from each patient were obtained from the same location on the lateral upper or lower arm. The DFS was based on the depth and % of dermal homogenization, size orientation and eosinophilia of fibers, and interstitial space between the fascicles in H&E -stained sections. The mRSS showed a significant improvement in 8/10 patients. The mean decrease in mRSS of 34 patients' (baseline 30.2) to final evaluation was 22.08 (-70.3%, and with a significant linear decrease over time, both p = < 0.0001). The DFS in 7 of 10 had ≥3 grades of reduction. 3 had a final DFS of 0 with reduction of dermal thickness, loss of homogenization thinning and straightening of the collagen bundles with an increase in interstitial space. The dermal-epidermal border remained straightened with loss of rete ridges and loss of elastica in the papillary dermis. The discordant final scores in patient 8, decrease in DFS without decrease in mRSS was likely related to localized improvement of skin at site of biopsy.

Conclusion:

A-HSCT for SSS leads to remodeling of dermal collagen with loss of sclerosis and corresponding improvements in the mRSS.

RESULTS: *Assessment of dermal fibrosis after A-HSCT for SSS*

Patient	Baseline mRSS/DFS	Final Score Year/mRss/DFS
1	35/3	2/3/1
2	16/3	6/0/0
3	40/5	5/10/0
4	26/4	1/18/3
5	19/4	5/1/1
6	20/5	4/7/3
7	30/4	4/8/0
8	48/5	4/42/1*
9	44/5	4/10/1
10	29/5	3/12/2

AUTOLOGOUS TRANSPLANTS

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PREVENTION OF MUCOSITIS IN AUTO BMT/STEM CELL TRANSPLANT PATIENTS

Klocke, J.[1], Cannon, M.[1], Gissenger, D.[1], Devoe, C.[1], John, V.[1], Bayer, R.-L.[1] [1]North Shore University Hospital, 300 Community Drive, Manhasset, NY.

It is estimated that 80% of patients who undergo high-dose chemotherapy plus or minus radiotherapy prior to transplantation develop mucositis. Mucositis is a painful complication, which can lead to poor nutrition, increased use of narcotics, dehydration, greater risk for infection and bacteremia, as well as altered quality of life. Patients can have oral ulceration, epigastric discomfort, diarrhea, rectal irritation, and bleeding. It is likely that the complications of mucositis can contribute to increased lenght of stay during stem cell transplantation.

The purpose of this study is to compare patients who received Kepivance(palifermin) as part of their treatment with patients that did not receive this medication during autologous stem cell trans-

plantation. We performed a retrospective analysis of 70 patients; 20 prior to the institution of Kepivance(palifermin), and 50 patients after. The preparative regimens include Melphalan, Busulfan & Etoposide, Cytoxan, BCNU, Etoposide, and Busulfan & Cytoxan.

The average length of stay for non-Kepivance patients was 32.3 days compared to 28 days in patients who received the drug. The severity of both oral and GI mucositis appeared to be less. 85% of non-Kepivance patients experienced diarrhea or rectal irritation, versus 52% with Kepivance. Neutropenic fever was noted in 95% of patients that did not receive the drug and 76% of the patients that did. There was a trend torward earlier engraftment in the Kepivance group.

Kepivance seems to have had a positive effect on our patients. This updated study suggests an improvement in mucositis symptoms with the use of Kepivance(palifermin). It appears that mucositis and its treatment contribute to the length of stay and costs of stem cell transplantation. Qualtiy of life for these patients can be greatly improved if mucositis is reduced during the course of stem cell transplantation.

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ROLE OF HIGH-DOSE CHEMOTHERAPY WITH AUTOLOGOUS STEM CELL TRANSPLANTATION IN PRIMARY SYSTEMIC AMYLOIDOSIS: A SYSTEMATIC REVIEW

Behera, M.[1], Kharfan-Dabaja, M.A.[1], Kumar, A.[1], Soares, H.P.[1], Djulbegovic, B.[1] [1]H. Lee Moffitt Cancer Center and Research Institute at the University of South Florida, Tampa, FL.

Background: Primary systemic amyloidosis (AL) is a rare plasma cell clonal disorder(8/million) characterized by extracellular deposits of material composed mainly of fragments of light chain immunoglobulin throughout a body. Standard chemotherapy (e.g. melphalan and prednisone) is associated with poor outcomes (typical median survival is between 12-18 months with less than 5% surviving 10 years). Autologous stem cell transplant (ASCT) has been increasingly advocated for the treatment of AL. However, it is uncertain whether ASCT is better than standard chemotherapy. To address this uncertainty, we undertook a systematic review/meta-analysis to evaluate the efficacy of high-dose chemotherapy and autologous stem-cell transplant (HSCT) versus conventional chemotherapy in patients with AL.

Methods: We searched for all published studies in Medline and Cochrane library databases. In addition, we hand searched for references. Studies were included if they were comparison trials of HSCT versus conventional chemotherapy, regardless of the trial design (e.g. randomized controlled trials [RCTs] or prospective studies with historical control). The studies were eligible if patients had biopsy proven AL with at least one major organ involved . Data were extracted on benefits as well as harms (overall survival, event-free survival, response, treatment related mortality, treatment-related morbidity).

Results: Out of 34 identified studies only 4 met the inclusion criteria for the current systematic review, two of which were RCTs and two were prospective non-randomized trials that included historical control. The ages of patients were in the range of 18-69 years. When we pooled all the data, we found that overall survival was similar for ASCT and conventional therapy arms [hazard ratio (HR) of 1.10 (95% CI 0.88, 1.36, p=0.4); no significant heterogeneity was found; p= 0.6]. Analysis of data according to design (randomized vs. non-randomized trials) resulted in similar results [HR=1.10 (95% CI 0.88, 1.37) and HR=0.98 (95% CI 0.29, 3.35), respectively]. The complete hematologic response was also similar between the 2 arms [OR= 1.38 (95% CI 0.67, 2.85; p=0.4].

Conclusion: The results from the meta-analysis indicate that there is no statistically significant difference between the treatment effects from high-dose chemotherapy with ASCT and conventional chemotherapy. Hence, the efficacy of ASCT in improving overall survival and complete hematologic response remains to be proven.

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DOSE DENSE DREIFACH* MELPHALAN100 FOR MULTIPLE MYELOMA

Berz, D.[1], McCormack, E.[2], Winer, E.[2], Karwan, P.[2], Colvin, G.[2], Rathore, R.[2], Larry, L.[2], Elfenbein, G.[2], Quesenberry, P.[2] [1]Brown University, Providence, RI; [2]Roger Williams Medical Center, Providence, RI.

Background: Tandem high dose melphalan therapy with autologous peripheral stem cell support has emerged as standard of care for patients without prohibitive comorbidities. Mucositis and gastrointestinal side effects are the most common extrahematologic side effects. Two previously published studies presented a triple transplant with a conditioning regimen melphalan 100mg/m2 (MEL100) with peripheral stem cell support every two to five months schedule for patients with prohibitive comorbidities for high dose tandem transplantation. We are presenting a novel approach that investigates the triple melphalan100/m2 approach on a dose dense, every three weeks schedule in a patient population without significant comorbidities.

Patients and methods: Thirteen standard or high risk patients with stageIII multiple myeloma were prospectively treated. This population contained eight patients with IgG clonality, 3 IgA, 1 nonsecretory and one light chain isotype. The induction regimens of the thirteen patients were heterogenous and included 5 VAD, 3 DCIE, 2 Thal/Dex, 2 CIE and 1 pulse decadron. Patients underwent peripheral blood leukopheresis, and these cells were divided into three equal sets and frozen. The patients were scheduled to receive Melphalan at 100mg/m2 on day -1, 20, and 41 and then the autologous infusions occurred at day 0, 21, and 42.

Results: All patients were able to receive all three cycles of the MEL100 regimen. Seven patients (54%) received the treatments on the every three week schedule; three treatments (23%) during the second cycle and six treatments (46%) of the third cycle had to be delayed a median of 6 and 4 days respectively. Three patients were managed completely in the outpatient setting, and the average total hospital stay for the three transplants was 18 days. Median progression free survival was 854 days (range 73 – 1571) and the overall survival of this cohort has yet to be reached. No patient had worse than grade II mucositis, and no serious adverse events were recorded.

Conclusions: Our regimen of three consecutive autologous peripheral stem cell transplants with a reduced dose of melphalan at 100mg/m2 given every three weeks is very well tolerated. The progression free survival and overall survival are similar and can be compared favorably with the standard tandem myeloma regimens. Our data is intriguing and further studies with larger numbers need to be performed to confirm these results. *German for triple.

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OUTCOMES ASSOCIATED WITH AGE IN PATIENTS WITH MALIGNANT LYMPHOMA RECEIVING AUTOLOGOUS STEM CELL TRANSPLANT

Beveridge, C.A.[1], Ershler, W.B.[2], Orloff, G.J.[1], Sheridan, M.J.[3], Shelton, M.V.[1] [1]Fairfax Northern Virginia Hematology-Oncology, PC, Fairfax, VA; [2]Institute for Advanced Studies in Aging, Washington, DC; [3]Inova Fairfax Hospital, Falls Church, VA.

Background and Rationale

Older age is frequently considered a contraindication to high dose therapy. We evaluated 32 auto-transplant patients with Malignant Lymphoma (ML) to determine whether outcomes for those ≥60 years of age differed from those <60 years of age.

Material and Methods

A retrospective assessment was undertaken of ML patients who were transplanted at Inova Fairfax Hospital from 2004-2006. All patients had Karnofsky performance scores of ≥80% and all were apheresed using a high volume technique and ideal body weight for calculations with either G-CSF (G) or G+GM-CSF, with a goal of 5×10^6/kg CD_{34} cells. Patients were treated with growth factor support using GM-CSF beginning day +4 through ANC recovery of 1000. Blood product replacement was standardized to transfuse for hemoglobin greater than 8gm/dl or platelet counts of >10,000/mm^3. Viability was performed using flow cytometry and propidium iodide. Continuous variables were analyzed as means and 95% confidence intervals, but p-values were produced using a Wilcoxon Rank Sum Test for non-normally distributed data. Categorical variables were analyzed using a Fisher's Exact Test.